REMARKS

In the most recent Office Action, the Examiner rejected claims 1, 3, 6-7, 10-11, 13, 16-17, and 21-43 under 35 USC § 103(a) as being unpatentable over Guire (4,979,959) in view of Marin, et al. (5,433,477). The Examiner contends that Guire discloses a vascular graft with a thrombogenic agent covalently bonded to its surface. The Examiner further contends that Marin, et al. teaches the use of a vascular graft as part of stent-graft and that the combination of these teachings would have been obvious to one skilled in the art.

The rejection under 35 USC § 103(a) is respectfully traversed. Guire does not disclose a vascular graft coated with a thrombogenic agent, such as thrombogenic collagen.

In the previous two responses submitted by Applicants, dated September 7, 2006 and May 26, 2006, the crux of the arguments were that Guire, while teaching thrombogenic coatings for some devices, does not teach thrombogenic coatings for vascular grafts. The Applicants base this conclusion on two main points (1) the text of Guire itself teaches away from a vascular graft coated with a thrombogenic agent and (2) that a person skilled in the art, based on the skill on knowledge pervasive at the time of the invention, would not read Guire to teach thrombogenic coated vascular grafts.

The Examiner contends that thrombogenic vascular grafts are disclosed based on the language found at Col. 1, lines 31-32; Col. 4, lines 28-45; Col. 2, lines 38-46; and Example 1 of Guire. With respect to the language of Columns 1, 2, and 4, Applicants concede that thrombogenic coated devices are disclosed. However, Applicants maintain that thrombogenic coated vascular grafts are not disclosed. Furthermore, the reference to

thrombogenic collagen at column 4, line 36 does not encompass the type IV collagen utilized in Example 1 since type IV is not thrombogenic (as is described more thoroughly below). Rather, this language must refer to other types, for example types I or III since these types are thrombogenic (See Barnes, et al. page 134 appended hereto in Appendix A). With respect to Example 1, Applicants maintain that only non-thrombogenic coated vascular grafts are disclosed because type IV collagen (as well as the other cell growth factors of Example 1) is non-thrombogenic. In Applicants' most recent response, evidence that type IV collagen is non-thrombogenic was submitted. Further evidence is submitted with this response.

In the Office Action, dated July 7, 2006, the Examiner cited the Parsons, et al. abstract. Parsons, et al. coated plastic surfaces with collagen types III, IV and V and exposed the coated surfaces to platelet-rich plasma. The ability of each of the three types of collagen to induce platelet adherence was evaluated. Parsons, et al. report that collagen types I, III, and IV caused greater platelet adherence than type V. Based on their findings, the authors concluded that type V collagen may be less thrombogenic than types I, III, or IV.

The Examiner cited the Parsons, et al. abstract for the proposition that type IV collagen is thrombogenic. Although the Examiner's use of this citation is instructive, it is not dispositive of the issue of whether type IV collagen is thrombogenic. Rather, further evaluation is necessary since a molecule's ability to induce platelet adherence, alone, is not sufficient to activate the thrombotic pathway.

Although the thrombotic pathway is complicated, only some major events need be reviewed to understand why type IV collagen is incapable of eliciting the pathway.

Packman, et al. describes the initial steps in thrombosis at page 212 of Volume 7 of Progress in Hemostasis and Thrombosis, appended hereto in Appendix A. As an initial step in the intrinsic thrombotic cascade, platelets adhere to an injured vessel wall. After attachment, the contents of the alpha and amine storage granules (in the platelets) are released. The contents of the granules act synergistically to cause platelet aggregation, which is defined as platelet-to-platelet adhesion. (See Packman, et al. pg 211). The aggregated platelets adhere to polymerizing fibrin, which stabilizes the aggregate and forms a hemostatic plug. To summarize, the thrombotic pathway consists of the following major platelet events: (1) platelet attachment, (2) platelet activation (granule release), (3) platelet aggregation, and (4) fibrin deposition.

It has been reported that while type IV collagen may be able to induce platelet adherence, it is not capable of initiating platelet aggregation and platelet granule release, which, as outlined above, are necessary steps in the thrombotic pathway. See: Packman, et al., page 22: collagen Type IV does not cause platelet aggregation or granule release; Alberio, et al. page 1212 in the abstract: collagen type IV does not induce granule release or upregulation of GP IIB/IIIA (a glycoprotein involved in platelet aggregation); Barnes M.J. and Scott D.M., pg. 134: type IV is not capable of inducing platelet aggregation unless it is chemically treated to form segment-long-spacing aggregates; and Trelstad, et al. page 502: type IV collagen does not elicit platelet aggregation or granule release (copies of which are appended hereto as Appendix A)

Because platelet aggregation and granule release are mandatory events in the thrombotic process and because type IV collagen is incapable of initiating these events, type IV collagen cannot be accurately classified as thrombogenic. In fact, it was this line

of reasoning that resulted in the United States government funding of the research that led to, in part, the invention disclosed in Guire. See Phase II Grant Application page 19 and Notice of Grant Award, appended hereto as Appendix B. As outlined in the Grant Application, the aim of the proposed research was to investigate the effectiveness of attaching cell adhesion factors to endovascular grafts to promote endothelialization as a means to control thrombosis and thereby improve patency rates of the grafts. (See Grant Application, Abstract of Research Plan, pg. 2). The grant applicants' stated that because an "immediate concern" with the use of factors that promote cell adhesion on vascular grafts was that those factors might also promote thrombosis, they selected factors that were non-thrombogenic. (see Grant Application page 19). The Applicant's selected collagen type IV as a cell adhesion factor that is non-thrombogenic (see Grant Application, page 19). In fact, the non-thrombogenic nature of type IV collagen was discussed in the Grant Application at page 19, where it is stated that type IV collagen is capable of inducing platelet attachment but that it does not promote platelet activation or aggregation and is therefore non-thrombogenic. The research proposed in the Grant Application, including the statement and explanation that type IV collagen is non-thrombogenic and therefore safe to attach to vascular grafts, was reviewed by a panel of government experts, deemed valuable, and funding granted (see Notice of Award attached in Appendix B).

Furthermore, as sworn to by Dr. Clapper in his affidavit (filed on October 6, 2005) and as evidenced by the statements in the Grant Application, at the time of the Guire invention and the present invention, it was the general consensus of the scientific community that hemostatic (aka thrombogenic) coatings on vascular grafts should be

avoided because of the risk of graft failure due to thrombosis. Therefore, one skilled in the art reading Guire would not interpret it to disclose thrombogenic coated vascular grafts. Rather, those skilled in the art would Guire and interpret it to disclose vascular grafts coated with non-thrombogenic factors (i.e., type IV collagen, albumin, etc.) and would assume that the disclosure of thrombogenic collagen at col. 4 line 39 was intended for devices other than vascular grafts.

The statements contained in the Grant Application and the arguments advanced by the Applicants, are supported by the statements made by Dr. Patrick E. Guire in an Affidavit appended hereto as Appendix C. Dr. Guire is the inventor of the claimed invention of U.S. Pat. 4,979,959 and a signatory of the Grant Application. In the affidavit, Dr. Guire states that at least one of the aims of the invention of Guire was to provide vascular grafts with factors that would promote cell adhesion without inducing thrombosis. To that end, Dr. Guire swears and deposes that he selected fibronectin and type IV collagen (among others) because of his understanding and the general consensus of the scientific community, that neither of those molecules would induce thrombosis. Dr. Guire also swears and deposes, that at the time of his invention, there was a strong general consensus that coating a vascular graft with a thrombogenic agent would be imprudent since thrombosis was the leading cause of graft failure and providing the surface of a graft with a thrombogenic agent would appear to only exacerbate that problem.

Dr. Guire further swears and deposes that there are applications for the employment of thrombogenic agents on device surfaces according to his invention. However, those applications did not include and were not intended to include vascular

grafts. Rather, Dr. Guire deposes, thrombogenic agents would have been considered more appropriate for devices such as sutures. Dr. Guire also points out that the specification of the '959 patent calls out sutures and thrombogenic collagen but does not specifically call out the combination of vascular grafts and a thrombogenic collagen.

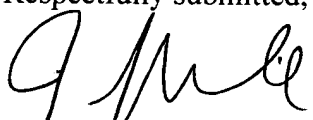
The pending claims are limited to a stent graft wherein the graft has a hemostatic bioactive agent. Guire does not teach a graft with a hemostatic agent. Applicant respectfully submits that claims 1, 3, 6-7, 10-11, 13, 16-17, and 21-43 are allowable over the cited art for at least the reasons outlined above and those contained in Applicants' previous two responses.

In light of the above, the Applicant respectfully submits that each of claims 1, 3, 6-7, 10-11, 13, 16-17, and 21-43 is in condition for allowance. Because these are the only claims pending in the application, prompt issuance of a Notice of Allowance in this case is courteously solicited.

If the Examiner feels that prosecution of the present application can be materially advanced by a telephonic interview, the undersigned would welcome a call at the number listed below.

Dated: 12/5/06

Respectfully submitted,



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